EUROPEAN UROLOGY XXX (2016) XXX–XXX

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Review – Prostate Cancer
Editorial by XXX on pp. x–y of this issue

Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis

Sean F. Mungovan[a,b,c,*], *Jaspreet S. Sandhu*[d], *Oguz Akin*[e], *Neil A. Smart*[b,f], *Petra L. Graham*[g], *Manish I. Patel*[h,i]

[a] *Westmead Private Physiotherapy Services, Westmead Private Hospital Sydney, Australia;* [b] *The Clinical Research Institute, Sydney, Australia;* [c] *Department of Physiotherapy, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Australia;* [d] *Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Centre, NY, USA;* [e] *Department of Radiology, Memorial Sloan-Kettering Cancer Centre, NY, USA;* [f] *School of Science & Technology, University of New England, Armidale, Australia;* [g] *Department of Statistics, Macquarie University, Australia;* [h] *Department of Urology, Westmead Hospital, Sydney, Australia;* [i] *Discipline of Surgery, Sydney Medical School, The University of Sydney, Australia*

Article info

Article history:
Accepted June 20, 2016

Associate Editor:
Christian Gratzke

Keywords:
Magnetic resonance imaging
Membranous urethral length
Membranous urethra
Meta-analysis
Prostate cancer
Systematic review
Urinary incontinence

Abstract

Context: Membranous urethral length (MUL) measured prior to radical prostatectomy (RP) has been identified as a factor that is associated with the recovery of continence following surgery.

Objective: To undertake a systematic review and meta-analysis of all studies reporting the effect of MUL on the recovery of continence following RP.

Evidence acquisition: A comprehensive search of PubMed, EMBASE, and Scopus databases up to September 2015 was performed. Thirteen studies comprising one randomized controlled trial and 12 cohort studies were selected for inclusion.

Evidence synthesis: Four studies (1738 patients) that reported hazard ratio results. Every extra millimeter (mm) of MUL was associated with a faster return to continence (hazard ratio: 1.05; 95% confidence interval [CI]: 1.02–1.08, $p < 0.001$). Eleven studies (6993 patients) reported the OR (OR) for the return to continence at one or more postoperative time points. MUL had a significant positive effect on continence recovery at 3 mo (OR: 1.08, 95% CI: 1.03–1.14, $p = 0.004$), 6 mo (OR: 1.12, 95% CI: 1.09–1.15, $p < 0.0001$). and 12 mo (OR: 1.12, 95% CI: 1.03–1.22, $p = 0.006$) following surgery. After adjusting for repeated measurements over time and studies with overlapping data, all OR data combined indicated that every extra millimeter of MUL was associated with significantly greater odds for return to continence (OR: 1.09, 95% CI: 1.05–1.15, $p < 0.001$).

Conclusions: A greater preoperative MUL is significantly and positively associated with a return to continence in men following RP. Magnetic resonance imaging measurement of MUL is recommended prior to RP.

Patient summary: We examined the effect that the length of a section of the urethra (called the membranous urethra) had on the recovery of continence after radical prostatectomy surgery. Our results indicate that measuring the length of the membranous urethra via magnetic resonance imaging before surgery may be useful to predict a longer period of urinary incontinence after surgery, or to explain a delay in achieving continence after surgery.

* Corresponding author. Westmead Private Physiotherapy Services, The Clinical Research Institute, Suite 6, 16–18 Mons Road, Westmead, NSW 2145, Australia. Tel. +61 2 9633 1035;
Fax: +61 2 9633 1641.
E-mail address: sean.mungovan@crinstitute.com.au (S.F. Mungovan).

http://dx.doi.org/10.1016/j.eururo.2016.06.023

Please cite this article in press as: Mungovan SF, et al. Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis. Eur Urol (2016), http://dx.doi.org/10.1016/j.eururo.2016.06.023

1. Introduction

Radical prostatectomy (RP) is the mainstay surgical treatment for localized prostate cancer. The aim of such surgery is to achieve oncologic control while preserving urinary continence and erectile function [1]. In the majority of patients, urinary incontinence (UI) following RP is a predictable consequence. Despite improvements in surgical techniques, the incidence of UI remains high, especially during the early postoperative period and the time to achieve continence (continence recovery) after RP, is variable. The variability in the rates of UI following RP remains one of the most significant functional complications with the potential for a negative impact on quality of life [2–4].

The prevalence of postprostatectomy UI varies according to the definition applied [5]. Encouragingly, despite the lack of a common and consistent working definition of continence, postoperative UI typically resolves gradually with time, with reports of significant improvement occurring up to 2 yr following RP [2,6,7]. The mechanism for the time dependent recovery of UI is not clearly understood.

Various preoperative prognostic patient-related risk factors that affect continence recovery have been reported. The preoperative length of the membranous urethra (MUL) which is measured via T2-weighted magnetic resonance imaging (MRI) images (Fig. 1), is one patient-related anatomical factor that has been reported to affect continence recovery following RP. A comprehensive understanding of MUL is potentially of value to clinicians when counselling patients in clinical practice prior to surgery and when explaining a delay in continence recovery following surgery. Also, given the recent technical advances that have led to the wider application of MRI technologies for the diagnosis and staging of prostate cancer [8], clinicians also have increased accessibility to obtain measurements of MUL prior to RP.

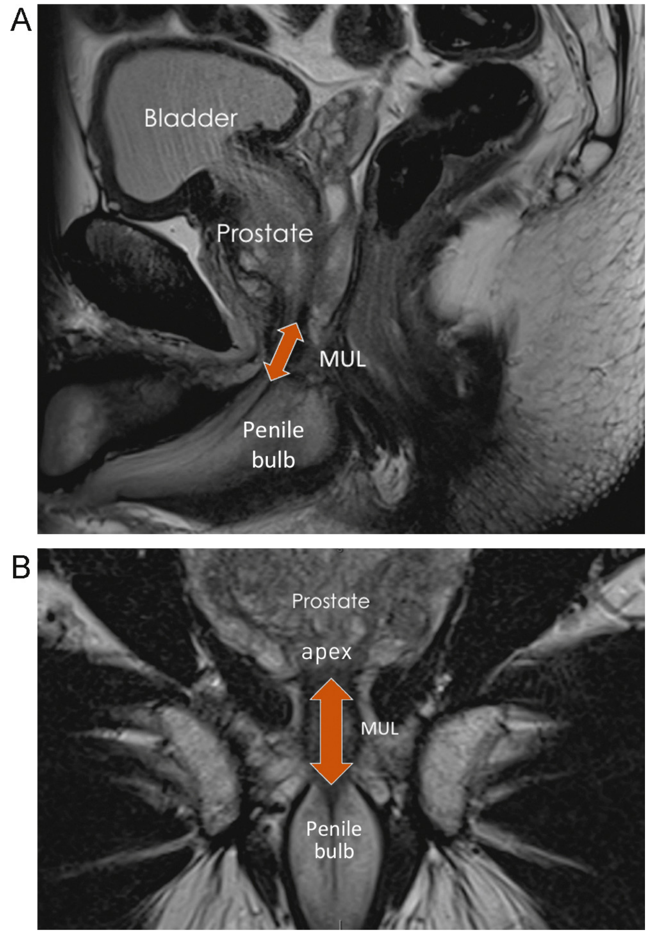

Fig. 1 – T2-weighted (A) sagittal and (B) coronal magnetic resonance images[a] for the measurement of membranous urethral length (MUL).
[a] The image was not taken from the studies included in this systematic review and meta-analysis.

2. Evidence acquisition

2.1. Objective

Our aim was to systematically review and meta-analyze studies reporting the prognostic value MUL measurements prior to RP for the recovery of continence.

2.2. Search strategy

We adopted the Preferred Reporting Items for Systematic Reviews and Meta-analysis [PRISMA] guidelines for our systematic review [9]. The PubMed, EMBASE, and Scopus databases were searched for relevant articles from the inception of each database until September 22, 2015. The systematic searches were formulated and conducted with the guidance of two health sciences librarians from the University of New England, Australia. The PubMed search strategy included a free-text protocol using the combined terms "prostatectomy OR radical prostatectomy AND urinary incontinence AND urethral length OR urethral volume OR membranous urethra" across the title and abstract fields of the records.

2.3. Study selection

After the removal of duplicates, two authors (SM and MP) screened all titles and abstracts independently to identify potentially relevant articles for eligibility. Full-text articles were obtained where there was insufficient information in the title or the abstract to determine eligibility. Reference lists were also manually searched to identify relevant articles not captured by the search strategies. Studies were included and excluded according to the criteria presented in Table 1. In all cases disagreements on eligibility were resolved by consensus.

2.4. Quality assessment

The methodological quality of each study was rated using the full version Downs and Black evaluation tool [10]. The tool consists of 27 questions across five sections: study quality (ten items), external validity (three items), internal validity bias (seven items), confounding selection bias (six items), and power of the study (one item) with an overall score out of a possible 30 points. The studies were

Table 1 – Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Men undergoing radical prostatectomy	Review articles and descriptive commentaries
Preoperative MRI completed	Animal studies
Preoperative MUL measurement undertaken	Conference abstracts or poster publications
Postoperative continence assessment completed	Published in a language other than English
English language	
Full journal article publication in a peer-reviewed journal	
A definition of MUL as the distance from the prostatic apex to the entry of the urethra into the penile bulb [42]	
A report of the relationship between preoperative MUL and postoperative continence status	

MRI = magnetic resonance imaging; MUL = membranous urethral length.

independently scored by two authors (SM and PG) with disagreements resolved by consensus.

2.5. Data extraction and synthesis

We used a standardized form to manually extract data relating to the: (1) the eligibility criteria, (2) study design and location (country and institution), (3) sample size, age, prostate-specific antigen, Gleason score, type of surgical approach (radical retro-pubic prostatectomy [RRP], robot assisted radical prostatectomy [RARP], and laparoscopic radical prostatectomy [LRP]), (4) MRI equipment and procedural characteristics for the measurement of MUL, (5) the definition, method of assessment, and the time points used for UI assessment, and (6) the measures of the risk of continence recovery (OR and/or hazard ratio). Data were independently extracted by two authors (SM and PG) with differences resolved by consensus. Authors of the studies identified in our search were also contacted by email to provide clarification and/or additional data where necessary. Where standard deviations were not reported we used the methods described Wan et al [11] (2014) to estimate them.

2.6. Meta-analysis methods

Meta-analysis aimed to quantify the effect of MUL on either the hazard or odds of a return to continence. A DerSimonian and Laird [12] random-effects meta-analysis was undertaken to pool the hazard ratios or the ORs at each time point. Where studies from the same institution appear to have overlapping data, the study with the largest data set was used. Sensitivity analysis was then undertaken to determine whether use of the excluded study would alter the results substantially. Finally, a multivariate meta-regression of the ORs was undertaken. The multivariate model allowed all of the available data to be included in one analysis while adjusting for studies that reported results at multiple time points and studies that overlap via a random intercept for study and a random slope for time. Covariates including postoperative follow-up time, publication year, study completion year or country of study, continence definition, surgical approach, and MUL measurement methodology were explored in the multivariate meta-regression model to determine whether they explained the heterogeneity between studies. While it was of interest to perform Egger bias tests, there were too few studies to allow this [13].

3. Evidence synthesis

3.1. Literature search

Figure 2 presents the PRISMA flow diagram for the study selection process. The searches retrieved 235 citations. After the removal of duplicates and a review of abstracts and full-text articles, 13 studies were eligible for inclusion in this systematic review and meta-analysis [14–26]. All corresponding authors were contacted via email to provide clarification and/or additional data where necessary. We received responses from eight authors [14,16,19,21–24,26]. Coakley et al [26] provided their data allowing for the calculation of required hazard ratios and ORs.

3.2. Quality assessment

The thirteen studies consisted of one intervention trial (randomized controlled trial) and twelve cohort studies (three prospective and nine retrospective) representing four different countries and seven different institutions. The ratings of the quality of the methods of the individual studies are presented in Table 2. Overall the scores were generally high with 11 out of the thirteen studies achieving 21 points or more. Studies typically lost points for internal validity and confounding and selection bias because of questions which were aimed at randomized and intervention trials. The two studies with lower scores had a poorer quality reporting of results.

3.3. Characteristics of the studies included

3.3.1. Patient and surgical characteristics

The patient and surgical characteristics are presented in Table 3. The mean age reported across all studies ranged from 58.0 yr to 66.1 yr (range, 37–85 yr). A total of 1738 patients (780 RRP, 937 RARP, and 21 LRP) were included in the four studies reporting the hazard ratio for the recovery of continence [20,22,24,26]. For the study reporting the OR of a return to continence at 1 mo, a total of 872 patients (416 RRP and 456 RARP) were included [18], for the studies at 3 mo 2517 patients (571 RRP,

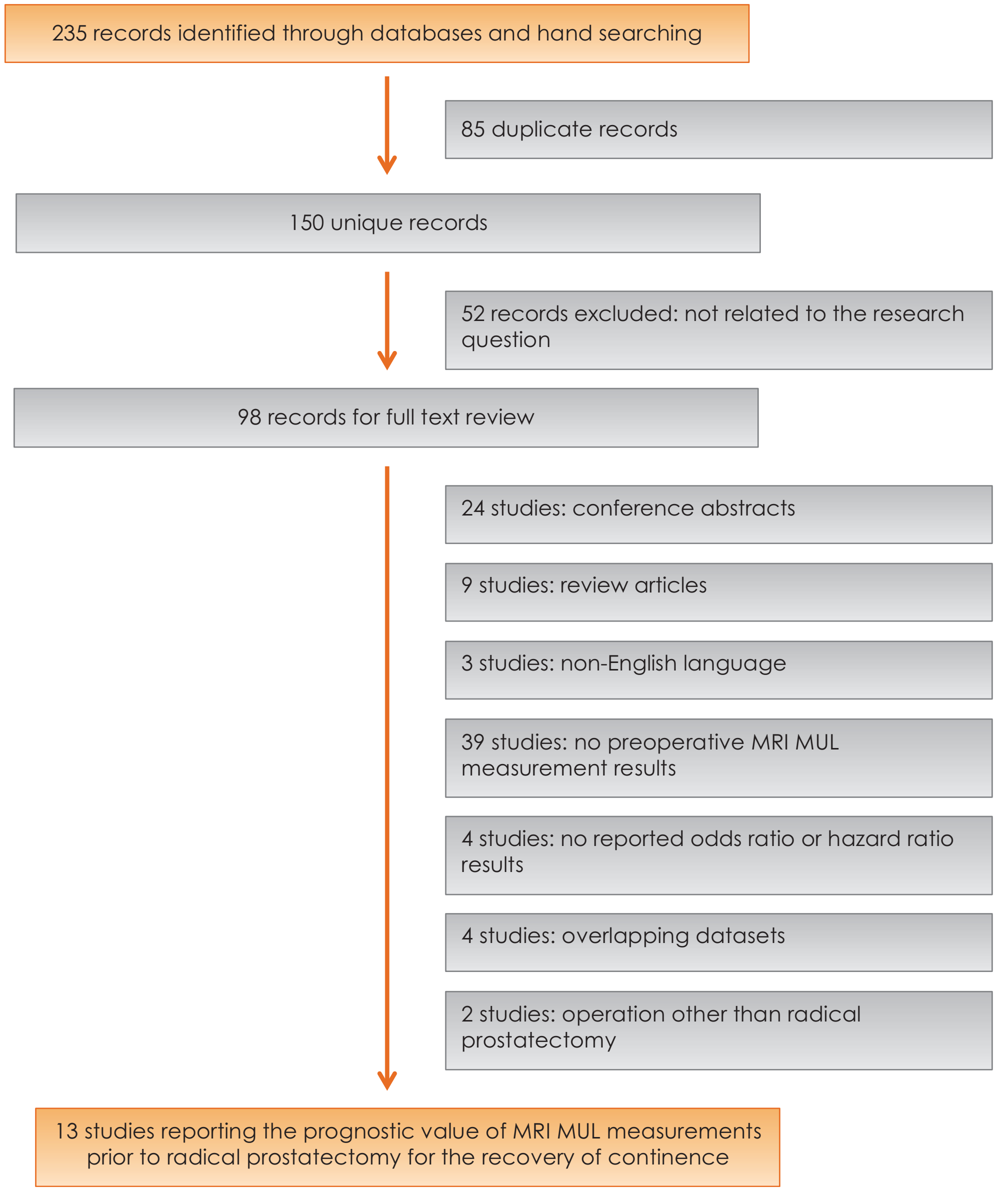

Fig. 2 – Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram presenting the outcome of the searches and selection of studies included in this review.
MRI = magnetic resonance imaging; MUL = membranous urethral length.

Table 2 – Downs and Black Quality Assessment Checklist evaluations for methodological quality (Downs and Black 1998)

Study	Reporting	External validity	Internal validity (bias)	Confounding and selection bias	Power	Total
Choi et al [14] 2015	10/11	3/3	6/7	4/6	1/1	24/28
Kadono et al [15]	8/11	3/3	5/7	2/6	0/1	18/28
Matsushita et al [16] 2015	11/11	3/3	5/7	3/6	0/1	22/28
Tienza et al [17] 2015	10/11	3/3	5/7	3/6	0/1	21/28
Jeong et al [18] 2014	10/11	3/3	5/7	3/6	0/1	21/28
Lee et al [19] 2014	10/11	3/3	5/7	3/6	0/1	21/28
Jeong et al [20] 2013	10/11	3/3	5/7	3/6	0/1	21/28
Lee et al [21] 2013	11/11	3/3	5/7	3/6	0/1	22/28
Kim et al [22] 2011	11/11	3/3	6/7	3/6	0/1	23/28
Lim et al [23] 2012	11/11	3/3	5/7	3/6	0/1	22/28
Paparel et al [24] 2009	11/11	3/3	5/7	3/6	0/1	22/28
Lee et al [25] 2006	10/11	3/3	5/7	3/6	0/1	21/28
Coakley et al [26] 2002	8/11	3/3	5/7	3/6	0/1	19/28

Please cite this article in press as: Mungovan SF, et al. Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis. Eur Urol (2016), http://dx.doi.org/10.1016/j.eururo.2016.06.023

Table 3 – Study, patient, and surgical characteristics

Study	Study period	Country	Sample	Age, mean ± SD (yr)	Age range (yr)	BMI, mean ± SD (kg/m²)	Preoperative PSA, mean ± SD (ng/ml)	Gleason biopsy ≤6 (%)	Gleason Biopsy 7 (%)	Gleason Biopsy ≥8 (%)	RRP	RARP	LRP	Attempted nerve sparing: Bilateral	Unilateral	Neither
Choi et al [14] 2015	2012–2013	Korea	158	64.65 ± 7.32	42–80	24.6 ± 3	10.15 ± 12.28	21.5	61.4	17.1	0	158	0	119	19	20
Kadono et al [15] 2015	2011–2013	Japan	111	NR	NR	NR	NR	NR	NR	NR	0	111	0	NR	NR	NR
Matsushita et al [16] 2015	2001–2010	USA	2849	60.0 ± 7.44	NR	27.7 ± 4	5.33 ± 2.22	52.2	40.0	7.8	1487	431	931	2130	447	272
Tienza et al [17] 2015	2002–2011	Spain	550	63.5 ± 7	41–83	NR	9.3 ± 2.2	66.3	23.3	10.4	378	0	172	297[b]	297*	253
Jeong et al [18] 2014	2004–2011	Korea	872	65.6 ± 6.7	37–82	NR	12.0 ± 33.3	20.4[a]	72.2[a]	7.3[a]	416	456	0	439	95	338
Lee et al [19] 2014	2007–2013	Korea	1011	65.6 ± 6.7	39–82	24.4 ± 3	12.8 ± 32.7	46.2	37.8	16.0	0	1011	0	638	112	261
Jeong et al [20] 2013	2006–2010	Korea	731	66.1 ± 7.0	41–85	24.2 ± 3	12.8 ± 41.6	19.3[a]	67.9[a]	12.9[a]	308	409	14	323	45	363
Lee et al [21] 2013	2007–2012	Korea	249	66.0 ± 6.0	49–78	23.3 ± 3	13.2 ± 14.4	47.0	39.0	14	0	0	249	100	54	95
Kim et al [22] 2011	2007–2010	Korea	763	64.9 ± 6.7	42–80	24.7 ± 3	11.7 ± 18.1	41.8	32.2	25.2	235	528	0	359	136	268
Lim et al [23] 2012	2005–2010	Korea	94	65.1 ± 5.8	49–77	23.7 ± 2	9.7 ± 7.4	55.3	31.9	12.8	94	0	0	39	25	30
Paparel et al [24] 2009	1999–2006	USA	64	60.7 ± 8.2	NR	NR	9.4 ± 6.0	8.0	50.0	28	57	0	7	25	15	7
Lee et al [25] 2006	2004–2005	Korea	156	65.9 ± 6.2	48–78	NR	10.8 ± 18.7	30.8	61.5	7.7	156	0	0	96[b]	96*	60
Coakley et al [26] 2002	1999–2001	USA	180	58.0 ± 7.0	40–74	NR	6.92 ± 7.34	NR	NR	NR	180	0	0	134[b]	134*	46

[a] Gleason pathological.
[b] Reported overall nerve sparing.
BMI = body mass index; LRP = laparoscopic radical prostatectomy; NR = not reported; PSA = prostate-specific antigen; RARP = robot-assisted radical prostatectomy; RRP = radical retropubic prostatectomy; SD = standard deviation.

1697 RARP, and 249 LRP) were included [14,19,21,22,25,26], at 6 mo 3187 patients (1667 RRP, 589 RARP, and 931 LRP) were included [14,16,26], and at 12 mo 4656 patients (2555 RRP, 998 RARP, and 1103 LRP) were included [15–18,23,26].

3.4. MRI equipment and MUL measurement procedures

The MRI procedures are presented in Table 4. The MUL was measured either by urologists, radiologists, or both specialties via consensus who were blinded to the patient's clinical data. MRI examinations were performed with the patient positioned in the supine position using 1.5T or 3T MRI units acquiring T2-weighted images which were used for MUL measurements. The use of an endorectal coil was used in four studies [16,21,24,26], not used in four studies [14,22,23,25], and not reported in five studies [15,17–20]. MUL was measured in either: (1) the coronal plane in six studies [16,19–21,25,26], (2) the sagittal plane in three studies [14,17,22], (3) the sagittal plane cross-referenced with the coronal plane in two studies [23,24], and (4) not reported in two studies [15,18].

3.4.1. MUL measurements

The MUL measurement results are presented in Table 4. The mean MUL measurements reported across all studies range from 10.4 mm to 14.5 mm; however, individual measurements of MUL were as small as 5 mm and as large as 34.3 mm.

3.5. Definition of UI

All studies reported a definition of continence and the method of assessment used. Twelve out of the 13 studies reported similar methods for the assessment of postoperative UI via direct patient questioning and/or the use of questionnaires about the perceived degree of UI, the absence of involuntary leakage and/or the use of absorbent products including pads and/or drip collectors [14,16–26]. Eight studies used pad-free status or the use of a security liner [14,16,18,21–25], two studies defined continence as 0–1 pad use [19,20], and two studies used a patient report of complete continence [17,26]. There was only one study [15] that used a 24-h pad test to define continence with a strict definition applied (pad weight gain not exceeding a mean of 2 g/d for 3 consecutive d).

3.6. Outcomes

The outcome reported by each study (hazard of return to continence and/or odds of return to continence) is shown in Table 5. Most studies reported ORs at one or more time points with two studies providing both hazard ratios and ORs (via correspondence with Coakley et al) [26].

3.6.1. The risk of return to continence

Four studies [20,22,24,26] (1738 patients) reported the hazard ratio associated with MUL and the return to continence (Fig. 3). Each of the studies indicated that a

Table 4 – Magnetic resonance imaging (MRI) and membranous urethral length (MUL) measurement procedures

	MRI equipment	Use of an endorectal coil	Professional measuring MUL	Plane used for MUL measurement	Were the assessor(s) blinded to patient continence data when measuring the MUL	MUL, mean ± SD (mm)	MUL range (mm)
Choi et al [14] 2015	3T	No	Urologist	Sagittal	Yes	11.9 ± 2.5	5–23
Kadono et al [15] 2015	NR	NR	NR	NR	NR	NR	NR
Matsushita et al [16] 2015	1.5 and 3T	Yes	Radiologist	Coronal	Yes	12.3 ± 3.7	10, 15[a]
Tienza et al [17] 2015	1.5T	NR	Radiologist	Sagittal	Yes	14.3 ± 4.5	6.7–34.3
Jeong et al [18] 2014	1.5T	NR	NR	NR	NR	12.8 ± 2.75	5–23
Lee et al [19] 2014	1.5T	NR	2 radiologists	Coronal	Yes	12.3 ± 2.5	5–21.5
Jeong et al [20] 2013	1.5T	NR	2 radiologists	Coronal	NR	12.8 ± 2.7	6–23
Lee et al [21] 2013	1.5T	Yes	Urologist	Coronal	Yes	11.9 ± 2.5	5.6–20.5
Kim et al [22] 2011	1.5T	No	Urologist	Sagittal	Yes	11.2 ± 3.1	5–23
Lim et al [23] 2012	NR	No	Radiologist	Sagittal cross-referenced with coronal	Yes	10.4 ± 3.8	NR
Paparel et al [24] 2009	1.5T	Yes	Radiologist and urologist by consensus	Sagittal cross-referenced with coronal	Yes	13.3 ± 3	6–21
Lee et al [25] 2006	1.5T	No	2 radiologists	Coronal	Yes	NR	NR
Coakley et al [26] 2002	1.5T	Yes	2 radiologists	Coronal	Yes	14.5 ± 3.5	6–24

[a] Interquartile range.
NR = not reported; SD = standard deviation; T = Tesla.

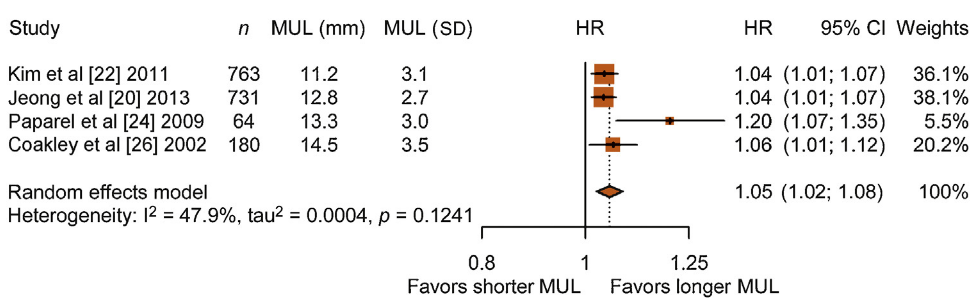

Fig. 3 – Forest plot of the risk of return to continence.
CI = confidence interval; HR = hazard ratio; MUL = membranous urethral length; SD = standard deviation.

greater MUL was significantly associated with a faster return to continence. Overall, the combined hazard ratio indicated a significant positive effect of greater MUL (hazard ratio: 1.05; 95% confidence interval [CI]: 1.02–1.08, $p < 0.001$). There was no evidence of heterogeneity between the studies ($p = 0.1241$).

3.6.2. Return to continence at 1 mo

One study [18] (872 patients) reported the OR for the return to continence at 1 mo. This study found a significant positive effect of greater MUL on the odds of return to continence (OR: 1.16, 95% CI: 1.09–1.23, $p < 0.001$).

3.6.3. Return to continence at 3 mo

Six studies [14,19,21,22,25,26] (2517 patients) reported ORs on return to continence at 3 mo (Fig. 4). All but one of the six studies found a significant positive effect of a greater MUL on the odds of return to continence. Figure 4 shows the results separated by whether or not the MUL was dichotomized. For each grouping and overall, a greater MUL is associated with significantly greater odds of return to continence by 3 mo (OR: 1.08, 95% CI: 1.03–1.14, $p = 0.004$). Sensitivity analysis using Jeong et al [18] in place of Lee et al [25] and Lee et al [19] because of a possible overlap in patients indicated very similar pooled results (OR: 1.10, 95% CI: 1.04–1.18). There was significant heterogeneity ($p = 0.0005$) that is not explained by whether or not MUL length is dichotomized.

3.6.4. Return to continence at 6 mo

Three studies (3187 patients) reported the odds of return to continence at 6 mo [14,16,26] (Fig. 5). Two of these studies, both with smaller sample sizes [14,26], had 95% confidence intervals that included one (ie, it was not significant); however, point estimates consistently indicated a positive effect on return to continence with a greater MUL length. The third study [16] comprises a large cohort of patients and is highly significant. Overall, pooled results show a significant positive effect of a greater MUL on the odds of return to continence at 6 m (OR: 1.12, 95% CI: 1.09–1.15, $p < 0.001$).

Please cite this article in press as: Mungovan SF, et al. Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis. Eur Urol (2016), http://dx.doi.org/10.1016/j.eururo.2016.06.023

Table 5 – The definition and assessment of urinary incontinence and continence recovery

	Definition of continence	Continence assessment method used	Overall continence recovery	Return to continence at 1 mo	Return to continence at 3 mo	Return to continence at 6 mo	Return to continence at 12 mo
Choi et al [14] 2015	Pad free	Expanded Prostate Index Composite questionnaire			Odds ratio	Odds ratio	
Kadono et al [15] 2015	Pad weight gain not exceeding a mean of 2 g/d for 3 consecutive d	24-h pad test					Odds ratio
Matsushita et al [16] 2015	No pad/no security pad	Institutional 5 point				Odds ratio	Odds ratio
Tienza et al [17] 2015	No complaint of involuntary urination	Patient interview and ICIQ-SF					Odds ratio
Jeong et al [18] 2014	Wearing no pad or the occasional security pad	Patient reported pad use		Odds ratio	Odds ratio		Odds ratio
Lee et al [19] 2014	0 pad/d or 0–1 pad/d for protection	Patient interview including by telephone as required			Odds ratio		
Jeong et al [20] 2013	0–1 pads/d	Question 5 of the Expanded Prostate Index Composite questionnaire	Hazard ratio				
Lee et al [21] 2013	Pad free	Patient interview in outpatient clinic regarding pad usage. Telephone interview if required			Odds ratio		
Kim et al [22] 2011	Pad free	Expanded Prostate Index Composite questionnaire and patient interview	Hazard ratio		Odds ratio		
Lim et al [23] 2012	Zero pad use or the use of a liner for security reasons only	Outpatient interview about pad usage					Odds ratio
Paparel et al [24] 2009	Patient reported complete continence using no pad or protection for 6 wk	Institutional 5 point scale	Hazard ratio				
Lee et al [25] 2006	Pad free with the feeling of complete urinary control	Patient interview including by telephone as required			Odds ratio		
Coakley et al [26] 2002	Complete continence	Institutional 5 point scale	Hazard ratio		Odds ratio	Odds ratio	Odds ratio

ICIQ-SF = International Consultation on Incontinence Questionnaire—Short Form.

3.6.5. Return to continence at 12 mo

Six studies (4656 patients) reported a return to continence at 12 mo [15–18,23,26] (Fig. 6). The studies were presented by whether MUL was dichotomized for analysis. The point estimate for the odds of return to continence was large for the study in which MUL had been dichotomized [23]. The studies that have not have dichotomized MUL have smaller point estimates of the OR. Most (five out of six) of the studies [16–18,23,26] showed a significant positive effect of greater MUL on the odds of return to continence at 12 mo and the overall pooled OR indicated a significant positive relationship between MUL length and return to continence (OR: 1.12, 95%CI: 1.03–1.22, $p = 0.006$).

3.7. *Subgroup analyses*

Subgroup analysis was completed to determine whether the heterogeneity between studies could be related to: (1) continence definition, (2) surgical approach, or (3) the MRI method used to measure MUL. The number of studies reporting the MUL related odds for the return to continence at 3 mo ($n = 6$) [14,19,21,22,25,26] and 12 mo ($n = 6$) [15–18,23,26] permitted the meta-analyses by subgroupings within each of these three factors of interest. For continence definition (pad free, 0–1 pad, 24-h pad test, or no complaint of incontinence) the results are mixed and the MUL odds of return to continence at 3 mo or 12 mo is not related to continence definition (Supplementary Figs. 1 and 2). Studies grouped by surgical approach (RRP, RARP, LRP, or a combination of surgical approaches) are also inconclusive with no difference between these subgroups for the MUL odds of return to continence at 3 mo and 12 mo (Supplementary Figs. 3 and 4). For the MRI method used to measure MUL (coronal, sagittal, or coronal cross-referenced with sagittal [combination]), the results are also variable and more studies are needed to determine conclusively if the odds of return to continence at 3 mo and 12 mo is related to the MRI method used to measure MUL (Supplementary Figs. 5 and 6).

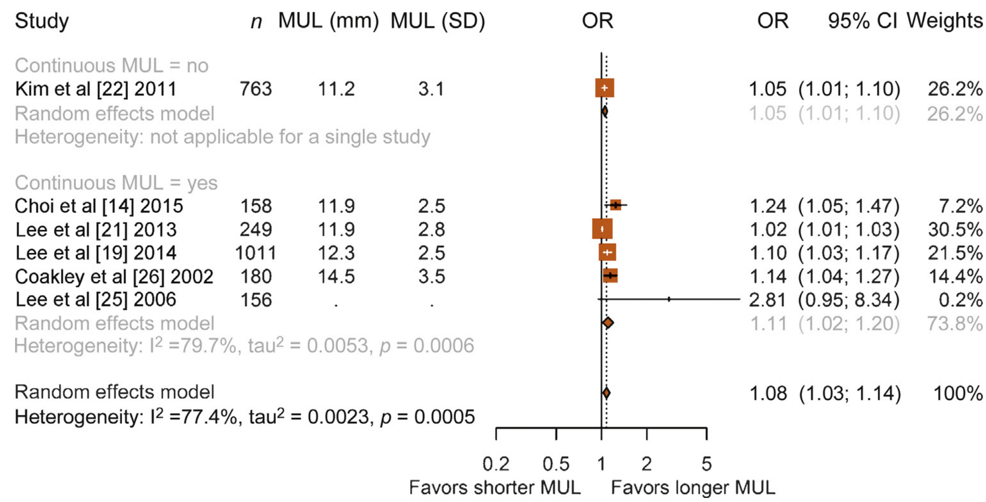

Fig. 4 – Forest plot of the odds of return to continence at 3 mo.
CI = confidence interval; OR = odds ratio; MUL = membranous urethral length; SD = standard deviation.

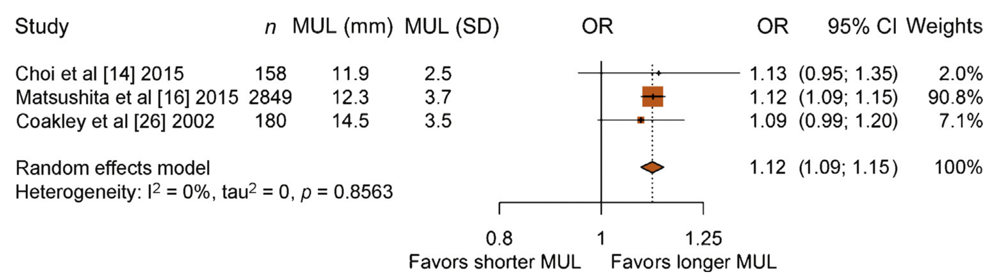

Fig. 5 – Forest plot of the odds of return to continence at 6 mo.
CI = confidence interval; OR = odds ratio; MUL = membranous urethral length; SD = standard deviation.

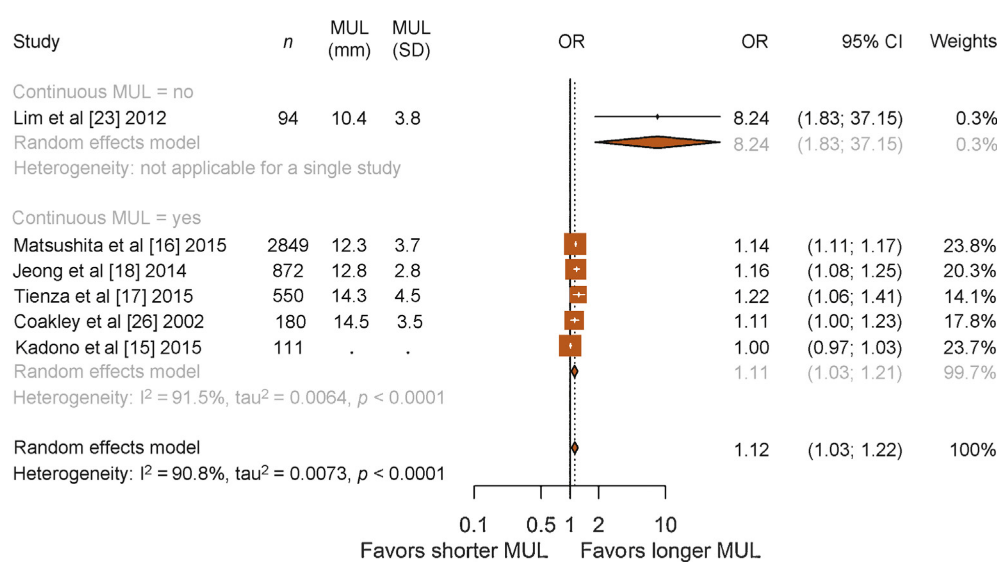

Fig. 6 – Forest plot of the odds of return to continence at 12 mo.
CI = confidence interval; OR = odds ratio; MUL = membranous urethral length; SD = standard deviation.

3.7.1. Multivariate meta-regression

All of the OR data were combined into a multivariate model using a random intercept to adjust for repeated measures by various studies and to control for studies with overlapping data [18,19] and a random slope over time. Overall for every extra millimeter of MUL the estimated odds of continence recovery is increased by between 5% and 15% (OR: 1.09, 95% CI: 1.05–1.15, $p < 0.001$). When this result is re-expressed for every extra 10 mm of MUL, the odds of continence recovery is increased by between 63% and 405% (OR: 2.37, 95% CI: 1.63–4.05). The only significant modifier of the MUL related odds of return to continence was the MRI method

Table 6 – Moderator *p* values

Predictor	*p* value
Time	0.495
Country	0.233
Completion date	0.286
Publication date	0.967
Continuous MUL (yes vs no)	0.693
Mean MUL	0.164
Continence definition	0.262
Surgical approach	0.140
MRI MUL measurement methodology	0.028

MRI = magnetic resonance imaging; MUL = membranous urethral length.

used to measure MUL ($p = 0.028$; Table 6). There was one study [23] that reported the odds of return to continence using the sagittal MRI image cross-referenced with the coronal MRI image to measure MUL. This study reported significantly higher odds of return to continence than those studies reporting the MUL measurement using: (1) the sagittal MRI image alone ($p = 0.010$), (2) the coronal MRI image alone ($p = 0.008$), or (3) studies that did not report the methodology used for MRI MUL measurement ($p = 0.009$). There was no evidence of a difference in effect between the sagittal and coronal MRI methods for MUL measurement ($p = 0.268$). Given that only one study [23] used the sagittal plane cross-referenced with the coronal plane method, the significant difference between this study and the others should be interpreted with caution.

4. Conclusions

To our knowledge, this is the first systematic review and meta-analysis that has investigated preoperative MUL as a prognostic risk factor for overall continence recovery and recovery at 1 mo, 3 mo, 6 mo, and 12 mo specifically. The key finding is that a greater preoperative MUL has a significant positive effect on overall time to continence recovery (pooling the hazard ratios) and continence recovery (pooling the ORs) at 3 mo, 6 mo, and 12 mo following RP. The analyses undertaken represents a small but significant positive effect of an extra millimeter in preoperative MUL on return to continence (ie, OR: 1.09, 95% CI: 1.05–1.15 from the multivariate model). Given the anatomical variation in the MUL measurements that have been reported (as small as 5 mm and as large as 34.3 mm), when this OR result is re-expressed as the OR for an extra 10 mm in preoperative MUL on the return to continence we obtained an OR of 2.37 with 95% CI: 1.63–4.05. This clearly indicates that with an extra centimeter of MUL the odds of return to continence are more than 200% more likely than for a man with a shorter MUL.

This finding is important because the variability of the reported UI outcomes has been identified as a major concern for patients and an important point of discussion that clinicians have with patients preoperatively and postoperatively. The variability in UI outcomes following prostatectomy includes both the overall continence recovery and the time-to-achieve continence. The uncertainty associated with the trajectory of the time course of recovery and the eventual outcome can potentially influence the decision to proceed with surgical management and can have a significant impact on the quality of life and psychosocial wellbeing following surgery [2–4]. The economic burden of postprostatectomy UI, including the cost of lost work productivity and associated management costs has also been reported [27–29]. Identifying patient-related factors including preoperative MUL is potentially important when counselling patients prior to and following surgery, in particular when setting expectations about the likely time course for the recovery of continence, and when discussing any delays in the recovery of continence. This systematic review supports the inclusion of preoperative MUL in these patient-centered discussions. This systematic review also supports MUL as a variable used in the development of predictive models for continence recovery after RP [16].

The comparison of studies reporting UI outcomes is also difficult due to the lack of a standardized definition of UI, inconsistent methods of assessment, and variable time points selected for patient follow-up. In our systematic review and meta-analysis we were able to pool 12 studies that used similar, clinically accessible, and frequently used approaches to continence definition and assessment and one study that used 24-h pad testing. We were also able to group studies according to identical time points for follow-up patient assessments. The use of patient-reported pad use and subjective reports of UI for continence definition and assessment following RP has, however, been questioned by some authors [3,32] and supported by others [7,30,31,33]. The approach used to define and assess UI after RP surgery in this systematic review, however, remains clinically accessible and widely used. There was only one study that used and reported 24-h pad test data with a strict and rarely clinically applied definition [15].

Our multivariate analysis indicates that follow-up time is not an important predictor of return to continence after adjusting for MUL; however, individual patient data analysis would help to better indicate the time course of recovery. Prostate removal by all surgical methods (RARP, RRP, and LRP) results in a change to the structure and function of the components of the urinary sphincter complex which are inherently related to the structure and function of the membranous urethra. The membranous urethra contains smooth muscle fibers along its entire length and is also surrounded by the rhabdosphincter (striated urethral sphincter) [33–35]. The rhabdosphincter is separated from the membranous urethra by a thin sheath of connective tissue and forms a muscular coat in an omega shaped loop around the membranous urethra [33–35]. The combined and coordinated functionality of the intact smooth muscle fibers and the rhabdosphincter has an important role in continence, contributing to maintaining and increasing urethral closure pressures [34,36]. Postoperative urethral sphincter insufficiency has been reported to affect continence outcomes following RP [33,34,36,37]. An increased length of MUL, which includes a greater amount of smooth muscle fibers and rhabdosphincter, potentially increases the length of the urethral pressure profile. Preoperative and postoperative conditioning of the

Please cite this article in press as: Mungovan SF, et al. Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis. Eur Urol (2016), http://dx.doi.org/10.1016/j.eururo.2016.06.023

rhabdoshpincter may also be optimized with a greater membranous urethral length incorporating a greater volume of muscle for training, further improving postoperative continence outcomes [38].

The importance of MUL has also been identified with modifications to and development of surgical techniques designed to improve continence outcomes after RP [39–41]. Many of these developments and modifications have centered on the preservation of the MUL and improved periurethral suspension for the protection and maintenance of the native continence system. A longer preoperative MUL may maximize the potential of these modifications to preserve the integrity and optimal functioning of the continence mechanism that is associated with the MUL. The preservation of MUL may, however, be limited by disease-related factors in order to achieve oncologic control.

The accessibility to acquire preoperative MUL measurements in clinical practice is greater with the wider application of preoperative MRI technologies for the diagnosis and staging of prostate cancer [8]. Standard multi-parametric MRI prostate imaging also includes the routine capturing of T2-weighted coronal and sagittal images. These T2-weighted images provide clinicians with the opportunity to obtain preoperative measurements of MUL as an inclusion to standard multi-parametric MRI radiological reporting procedures. Traditionally preoperative prostate MRI imaging has been undertaken using a 1.5T and 3-Tesla to 3T scanner and an endorectal coil. The application of a higher field strength (3-Tesla) and subsequent higher spatial resolution has resulted in a reduction in the use of endorectal coils, further increasing the accessibility of preoperative MRI scanning in clinical practice.

Despite a comprehensive search strategy and a rigorous approach to the study selection, the omission of relevant studies may have been possible. The inclusion of only English language manuscripts may also have excluded some relevant studies. The conclusions and recommendations contained within this review are based upon the synthesis and evaluation of twelve studies that have relied on patients reporting the degree of UI and pad usage for the assessment of postoperative UI and one study that used a 24-h pad test.

In conclusion, the preoperative measurement of MUL via MRI is recommended prior to RP to predict the recovery of UI after surgery or to explain a delay in achieving continence after surgery.

Author contributions: Sean F. Mungovan and Petra L. Graham had full access to all the data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Mungovan, Sandhu, Akin, Smart, Graham, Patel.
Acquisition of data: Mungovan, Smart, Graham, Patel.
Analysis and interpretation of data: Mungovan, Sandhu, Akin, Smart, Graham, Patel.
Drafting of the manuscript: Mungovan, Sandhu, Akin, Smart, Graham, Patel.
Critical revision of the manuscript for important intellectual content: Mungovan, Sandhu, Akin, Smart, Graham, Patel.
Statistical analysis: Graham.
Obtaining funding: None.
Administrative, technical, or material support: None.
Supervision: None.
Other: None.

Financial disclosures: Sean F. Mungovan certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

Acknowledgments: The authors acknowledge the support and assistance that was received for the search strategy from: L. Gurney (librarian) and C. Quilkey (librarian), University of New England; Kuan-Yin Lin (research assistant); and R. Fraser (research assistant), The Clinical Research Institute. Assistance was received for the preparation of the manuscript from C. Skowron and K. Sterns.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at .http://dx.doi.org/10.1016/j.eururo.2016.06.023.

References

[1] Patel VR, Abdul-Muhsin HM, Schatloff O, et al. Critical review of "pentafecta" outcomes after robot-assisted laparoscopic prostatectomy in high-volume centres. BJU Int 2011;108:1007–17.
[2] Punnen S, Cowan JE, Chan JM, Carroll PR, Cooperberg MR. Long-term health-related quality of life after primary treatment for localized prostate cancer: Results from the CaPSURE registry. Eur Urol 2015; 68:600–8.
[3] Liss MA, Osann K, Canvasser N, et al. Continence definition after radical prostatectomy using urinary quality of life: Evaluation of patient reported validated questionnaires. J Urol 2010;183:1464–8.
[4] Sanda MG, Dunn RL, Michalski J, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. N Engl J Med 2008;358:1250–61.
[5] Holm HV, Fossa SD, Hedlund H, Schultz A, Dahl AA. How should continence and incontinence after radical prostatectomy be evaluated? A prospective study of patient ratings and changes with time. J Urol 2014;192:1155–61.
[6] Lee JK, Assel M, Thong AE, et al. Unexpected long-term improvements in urinary and erectile function in a large cohort of men with self-reported outcomes following radical prostatectomy. Eur Urol 2015;68:899–905.
[7] Sacco E, Prayer-Galetti T, Pinto F, et al. Urinary incontinence after radical prostatectomy: incidence by definition, risk factors and temporal trend in a large series with a long-term follow-up. BJU Int 2006;97:1234–41.
[8] Sciarra A, Barentsz J, Bjartell A, et al. Advances in magnetic resonance imaging: how they are changing the management of prostate cancer. Eur Urol 2011;59:962–77.
[9] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339:b2700.
[10] Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomized and nonrandomized studies of health care interventions. J Epidemiol Community Health 1998;52:377–84.

[11] Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014;14:135.

[12] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.

[13] Higgins J, Green S. Cochrane handbook for systematic reviews of interentions. The Cochrane Collaboration 2011. http://handbook.cochrane.org.

[14] Choi SK, Park S, Ahn H. Randomized clinical trial of a bladder neck plication stitch during robot-assisted radical prostatectomy. Asian J Androl 2015;17:304–8.

[15] Kadono Y, Ueno S, Kadomoto S, et al. Use of preoperative factors including urodynamic evaluations and nerve-sparing status for predicting urinary continence recovery after robot-assisted radical prostatectomy: Nerve-sparing technique contributes to the reduction of postprostatectomy incontinence. Neurourol Urodyn. In press. http://dx.doi.org/10.1002/nau.22877.

[16] Matsushita K, Kent MT, Vickers AJ, et al. Preoperative predictive model of recovery of urinary continence after radical prostatectomy. BJU Int 2015;116:577–83.

[17] Tienza A, Hevia M, Benito A, Pascual JI, Zudaire JJ, Robles JE. MRI factors to predict urinary incontinence after retropubic/laparoscopic radical prostatectomy. Int Urol Nephrol 2015;47:1343–9.

[18] Jeong SJ, Yeon JS, Lee JK, et al. Development and validation of nomograms to predict the recovery of urinary continence after radical prostatectomy: Comparisons between immediate, early, and late continence. World J Urol 2014;32:437–44.

[19] Lee H, Kim K, Hwang SI, et al. Impact of prostatic apical shape and protrusion on early recovery of continence after robot-assisted radical prostatectomy. Urology 2014;84:844–9.

[20] Jeong CW, Oh JJ, Jeong SJ, et al. Effect of dorsal vascular complex size on the recovery of continence after radical prostatectomy. World J Urol 2013;31:383–8.

[21] Lee S, Yoon CJ, Park HJ, Lee JZ, Ha HK. The surgical procedure is the most important factor affecting continence recovery after laparoscopic radical prostatectomy. World J Mens Health 2013;31: 163–9.

[22] Kim SC, Song C, Kim W, et al. Factors determining functional outcomes after radical prostatectomy: robot-assisted versus retropubic. Eur Urolol 2011;60:413–9.

[23] Lim TJ, Lee JH, Lim JW, Moon SK, Jeon SH, Chang SG. Preoperative factors predictive of continence recovery after radical retropubic prostatectomy. Korean J Urol 2012;53:524–30.

[24] Paparel P, Akin O, Sandhu JS, et al. Recovery of urinary continence after radical prostatectomy: association with urethral length and urethral fibrosis measured by preoperative and postoperative endorectal magnetic resonance imaging. Eur Urol 2009;55: 629–37.

[25] Lee SE, Byun SS, Lee HJ, et al. Impact of variations in prostatic apex shape on early recovery of urinary continence after radical retropubic prostatectomy. Urology 2006;68:137–41.

[26] Coakley FV, Eberhardt S, Kattan MW, Wei DC, Scardino PT, Hricak H. Urinary continence after radical retropubic prostatectomy: relationship with membranous urethral length on preoperative endorectal magnetic resonance imaging. J Urol 2002;168:1032–5.

[27] Dahl S, Loge JH, Berge V, Dahl AA, Cvancarova M, Fossa SD. Influence of radical prostatectomy for prostate cancer on work status and working life 3 years after surgery. J Cancer Surviv 2015;9:172–9.

[28] Liberman D, Trinh QD, Jeldres C, Zorn KC. Is robotic surgery cost-effective: yes. Curr Opin Urol 2012;22:61–5.

[29] Jayadevappa R, Schwartz JS, Chhatre S, Gallo JJ, Wein AJ, Malkowicz SB. The burden of out-of-pocket and indirect costs of prostate cancer. Prostate 2010;70:1255–64.

[30] Nitti VW, Mourtzinos A, Brucker BM, Group SPTS. Correlation of patient perception of pad use with objective degree of incontinence measured by pad test in men with post-prostatectomy incontinence: the SUFU Pad Test Study. J Urol 2014;192:836–42.

[31] Haga N, Yanagida T, Yabe M, et al. Timing of urinary pad exchanges was the most important factor affecting quality of life in the early postoperative period after robot-assisted laparoscopic radical prostatectomy. J Endourol 2015;29:1044–51.

[32] Wei JT, Dunn RL, Marcovich R, Montie JE, Sanda MG. Prospective assessment of patient reported urinary continence after radical prostatectomy. J Urol 2000;164:744–8.

[33] Strasser H, Ninkovic M, Hess M, Bartsch G, Stenzl A. Anatomic and functional studies of the male and female urethral sphincter. World J Urol 2000;18:324–9.

[34] Strasser H, Pinggera GM, Gozzi C, et al. Three-dimensional transrectal ultrasound of the male urethral rhabdosphincter. World J Urol 2004;22:335–8.

[35] Dalpiaz O, Mitterberger M, Kerschbaumer A, Pinggera GM, Bartsch G, Strasser H. Anatomical approach for surgery of the male posterior urethra. BJU Int 2008;102:1448–51.

[36] Bentzon DN, Graugaard-Jensen C, Borre M. Urethral pressure profile 6 months after radical prostatectomy may be diagnostic of sphincteric incontinence: preliminary data after 12 months' follow-up. Scand J Urol Nephrol 2009;43:114–8.

[37] Gudziak MR, McGuire EJ, Gormley EA. Urodynamic assessment of urethral sphincter function in post-prostatectomy incontinence. J Urol 1996;156:1131–4.

[38] Chang JI, Lam V, Patel MI. Preoperative pelvic floor muscle exercise and postprostatectomy incontinence: A systematic review and meta-analysis. Eur Urol 2016;69:460–7.

[39] Rocco B, Gregori A, Stener S, et al. Posterior reconstruction of the rhabdosphincter allows a rapid recovery of continence after transperitoneal videolaparoscopic radical prostatectomy. Eur Urol 2007; 51:996–1003.

[40] Tewari A, Jhaveri J, Rao S, et al. Total reconstruction of the vesico-urethral junction. BJU Int 2008;101:871–7.

[41] Coelho RF, Chauhan S, Orvieto MA, et al. Influence of modified posterior reconstruction of the rhabdosphincter on early recovery of continence and anastomotic leakage rates after robot-assisted radical prostatectomy. Eur Urol 2011;59:72–80.

[42] Myers RP, Cahill DR, Devine RM, King BF. Anatomy of radical prostatectomy as defined by magnetic resonance imaging. J Urol 1998;159:2148–58.

Please cite this article in press as: Mungovan SF, et al. Preoperative Membranous Urethral Length Measurement and Continence Recovery Following Radical Prostatectomy: A Systematic Review and Meta-analysis. Eur Urol (2016), http://dx.doi.org/10.1016/j.eururo.2016.06.023